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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1653	7

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,095	ZUCHT ET AL.	
	Examin r	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 13-17* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 3 and 13-17 are pending.

Applicants' amendment filed March 25, 2003 (Paper No. 20) is acknowledged and applicants' response has been fully considered. Claims 6-12 have been cancelled, claim 3 remains withdrawn from consideration, and new claims 13-17 have been added. Thus, claims 13-17 and SEQ ID NO:22 are examined.

Objection Withdrawn

2. The previous objection to the specification regarding citing amino acid sequences without "SEQ ID NO:", and "R_1, R_3 independently represent NH_2", is withdrawn in view of applicants' amendment to the specification.

3. The previous rejection of claim 7 is withdrawn in view of applicants' cancellation of the claim.

Claim Rejections - 35 USC § 112

4. The previous rejection of claims 6-12 under 35 U.S.C.112, first and second paragraphs, is withdrawn in view of applicants' cancellation of the claim.

Informalities

The disclosure is objected to because of the following informalities:

5. The specification is objected to for "R_2, R_4 independently represent $CONH_2$" (page 3) since each amino acid in the peptide (HN-CH(R)-CO) has already contained the amino (NH) and carbonyl (CO) groups. It is incorrect to cite "R_2, R_4 independently represent $CONH_2$" for C-

terminal end of the peptide, it should be written as "R_2, R_4 independently represent NH_2". Appropriate correction is required.

Claim Objections

6. Claim 14 is objected to because the claim contains recitation of non-elected sequences.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 13-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for peptides with defined sequences such as SEQ ID NO:17 and SEQ ID NO:19 obtained from cow or human milk via a process of proteolytic cleavage and purification, and having bifidogenic properties; and a method of obtaining these peptides, does not reasonably provide enablement for a peptide obtained from cow or human milk via a process of proteolytic cleavage and purification, or, the N-terminal modified derivative or fragment of the peptide, which has bifidogenic property, wherein the amino acid sequence of the peptide is not defined; and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria, comprising administering the peptide to an individual. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 13-17 are directed to peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, the N-terminal modified derivatives or fragments thereof, which have bifidogenic properties (claims 13-15), a method of obtaining these peptides (claim

16), and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria (claim 17). The specification, however, only discloses cursory conclusions (pages 1-14) without data supporting the findings, which state that peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, or, their amidated, acetylated, sulfated, phosphorylated, glycosylated or oxidized derivatives or fragments thereof, would have bifidogenic properties (pages 1-2), and some sequences are listed as preferable embodiments (page 3). There are no indicia that the present application enables the full scope in view of peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, and the derivative or fragments thereof as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the derivatives or fragments of the peptides, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification only demonstrates certain peptides such as SEQ ID NOs: 17 (casein K-63-117) and 19 (neutrophile lactoferrin 20-67), and the oxidation product exhibit bifidogenic activity (Example 1, page 8). There are no other working examples indicating the claimed variants or methods in association with the claimed invention.

(3). The state of the prior art and relative skill of those in the art:

Proulx et al. (Lait 74, 139-152 (1994)) indicate the casein hydrolysates produced by three proteolytic enzymes have bifidogenic activity. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identities of the peptide derivatives or fragments, and the treating conditions for promoting the growth of bifidobacteria in individual using the peptide to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, the derivative or fragments thereof, which have bifidogenic properties, a method of obtaining these peptides, and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria. The specification indicates the peptides isolated and purified from cow milk or human milk can promote the growth of desired bacteria such as bifidobacteria more than that of other bacteria or by selectively inhibiting the undesired bacteria, which is defined as "bifidogenic" (page 3, first paragraph), and the peptide can be contained in medicaments or in food, and further asserts the peptides are suitable for treating diseases caused by various microorganisms (pages 4-5). The Examples have only

indicated the isolation and purification of certain peptides having bifidogenic properties (Example 1, page 8), the method of monitoring the growth-regulating activity on *E. coli* (Example 2), the method of monitoring the growth-regulating activity on *Bifidobacterium bifidum* (Example 3), and a formula to define bifidogenic activity (Example 4). However, the specification has not identified any N-terminal modified derivative or fragment having the bifidogenic property, and there are no working examples indicating the bifidogenic activities of these derivatives or fragments. Furthermore, there is no *in vitro* or *in vivo* data indicating the peptide, the derivative or fragment is effective in promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria in individual. Therefore, it is necessary to have additional guidance on the identity of the peptide derivatives or fragments, and the treating conditions such as dose for promoting the growth of bifidobacteria in individual, and to carry out further experimentation to assess the effect of the peptides with bifidogenic property.

(5). Predictability or unpredictability of the art:

The claims encompass many peptide variants and the treating conditions such as the dose for various compounds are not described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

The scope of the claims includes many structural variants, however the specification has not demonstrated the identities and the use of these variants. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, and the guidance and the teaching in the specification is

limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the bifidogenic effect of the claimed invention.

8. Claims 13-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 13-17 are directed to peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, the N-terminal modified derivative or fragments thereof, which have bifidogenic properties, a method of obtaining these peptides, and a method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria. The specification indicates that peptides obtained from cow or human milk via a process of proteolytic cleavage and purification, or, their amidated, acetylated, sulfated, phosphorylated, glycosylated or oxidized derivatives or fragments thereof, would have bifidogenic properties (pages 1-2), and some sequences are listed as preferable embodiments (page 3). The specification further asserts that SEQ ID NOs: 17 (casein K-63-117) and 19 (neutrophile lactoferrin 20-67), and the oxidation product exhibit bifidogenic activity (Example 1, page 8). However, the specification has not identified any fragment of a bifidogenic peptide. There is no disclosure indicating the N-terminal modified derivatives or fragments of the peptides are functional. Without guidance on structure to function/activity, one skilled in the art would not know which region or residue of the peptide is essential for function/activity and how to identify a functional peptide. The lack of a structure to function/activity relationship and the lack of representative species for the N-terminal modified derivatives or fragments of the peptides

having bifidogenic properties as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 14, 15 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 14 is indefinite because of the use of the term "a fragment thereof". The term "a fragment thereof" renders the claim indefinite, it is unclear what amino acid sequence the fragment has. Claim 14 is also indefinite for using the term "R_2, R_4 independently represent $CONH_2$". It is not clear what group at the C-terminal end of the peptide have since each amino acid (HN-CH(R)-CO) in the peptide has already contained the amino (NH) and carbonyl (CO) groups.

13. Claim 15 is indefinite because the claim depends from a cancelled claim.

14. Claim 17 is indefinite because the claim lacks essential steps in the method of promoting the growth of bifidobacteria or inhibiting the growth of non-bifidobacteria. The omitted step is the effective amount of the peptide used and the outcome of the treatment.

In response to various rejections under 35 U.S.C. 112, first and second paragraphs, applicants request reconsideration of all the rejections and objections in view of the amendment

and the specification (page 6 of the response). The response is not found persuasive because all the issues regarding the rejections and objections have not been addressed as indicated above.

Conclusion

15. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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June 6, 2003

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